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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,571	12/03/2001	Ian Tomlinson	8039/1125	6655

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/008,571	TOMLINSON ET AL.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/888,313.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application and Claims Status

1. Applicant's amendment and response filed 07/10/2006 are acknowledged and entered. Claims 1-10, 12-16, and 18-53 have been cancelled. Claims 11 and 17 have been amended.

2. Claims 11 and 17 are pending.

3. Claims 11 and 17 are under consideration in this Office Action.

Response to Amendment

4. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Status of Claim(s) Objection(s) and /or Rejection(s)

5. The rejections of claims 11 and 17 under 35 USC 112, second paragraph, as being indefinite have been withdrawn in light of applicant's amendments of claims 11 and 19.

6. The rejection of claims 11 and 17 under 35 USC 103(a) as being obvious over Winkler et al. (US Patent 5,677,195) and Wagner et al. (US Patent 6,329,209 B1) has been withdrawn in view of applicant's arguments (see page 6, filed 07/10/2006).

7. However, upon further consideration, a new ground(s) of rejection is made regarding written description of two-chain and three-chain polypeptides. Therefore, this Office Action is a Non-Final Office Action and the examiner apologizes for any inconvenience.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant invention recites a method for creating a combinatorial library of two-chain polypeptides, wherein each two-chain polypeptide of said library comprises one member of a first repertoire of single chain polypeptides and one member of a second repertoire of single chain polypeptides. The method comprises the step of providing an array comprising a solid surface that includes said first repertoire of single chain polypeptides present on the solid-surface in a first series of continuous lines that do not intersect with each other, and said second repertoires of single chain polypeptides are present on a the solid surface in a second series of continuous lines that do not intersect with each other, wherein each line of the first series of lines intersects with each line of the second series of line such that members of the first repertoire are

juxtaposed with members of the second repertoire, thereby generating two-chain polypeptides at the intersection of said first and second series of lines, thereby creating a combinatorial library of two-chain polypeptides.

With regard to the written description requirement, the attention of the Applicant is directed *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985)(quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

Additionally, it is noted that written description is legally distinct from enablement: "Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co.* And also *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

In this case, the instant invention claimed a method for making a broad genus of compositions, i.e. a combinatorial library of two-chain polypeptides, which represents enormous scope because the claims do not place any limitations on the number of atoms, i.e. binding moieties, types of atoms or the way in which said atoms can be connected together to form such a compound and/or composition (two-chain polypeptides). Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope encompassing virtually every known class and subclass of compounds (two-chain polypeptides). For example, Lehninger et al. disclose each protein has a specific chemical or structural function such that each protein has a unique three-dimensional structure (pg. 160, lines 4-6; fig. 7-1). The three-dimensional structure of a protein is determined by its amino acid, but the relationship between the amino acid sequence and the three-dimensional structure is an intricate puzzle that has yet to be solved in detail (see pg. 160, lines 14-29). Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope encompassing virtually every known class and subclass of compounds, i.e. two-chain polypeptides would encompass protein dimers such as leucine zipper, G protein βγ-subunit dimer, and Kinesin wherein these protein dimers are structurally and functionally distinct from each other.

Consequently, the scope of the instant claimed compositions, i.e. two-chain polypeptides, includes an enormous number of structural variants.

In contrast, the instant specification provided a broad generic definition of the term "polypeptides" (see pg. 28, lines 7-27) and is silent regarding the term "two-chain polypeptides". The instant specification one example is directed to the method for making a high-density array

of antibodies using antibody heavy chains (V_H) and antibody light chains (V_L) (see specification Example 5, pgs 54-55).

Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding adequate disclosure. For adequate disclosure, like enablement, requires ***representative examples***, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is ***substantial variation within the genus***, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

Here, the instant specification has only provided one working example of the claimed invention (i.e. the method of making an array of antibodies using antibody heavy chains (V_H) and antibody light chains (V_L)). Thus, a person of skill in the art would not believe that Applicants were in possession of a genus that encompasses virtually an infinite number of compounds and/or compositions encompassing every class and subclass of the instant claimed method for making a combinatorial library of two-chain polypeptides, i.e. the product produce by the instant claimed method encompasses any protein dimers.

Accordingly, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the claimed invention. The instant specification and claims do not provide any guidance as to what changes should be made to extend the instant specification one example to the infinite number of possibilities that are currently being claimed composition, i.e. two-chain polypeptides, for use in the instant claimed method. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, the instant specification single example is insufficient to describe the enormous genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the instant claimed method for making a combinatorial library of two-chain polypeptides, i.e. the product produce by the instant claimed method encompasses any protein dimers. Therefore, only the method of making an array of antibodies using antibody heavy chains (V_H) and antibody light chains (V_L), but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

10. Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant invention recites a method for creating a combinatorial library of three-chain polypeptides, wherein each three-chain polypeptide of said library comprises one member of a first repertoire of single chain polypeptides, one member of a second repertoire of single chain polypeptides, and one member of a third repertoire of single chain polypeptides. The method comprises the step of providing an array, comprising a solid surface ' that includes said first repertoire of single-chain polypeptides present on the solid surface in a first series of continuous lines that do not intersect with each other, said second repertoire of single-chain polypeptides present on the solid surface in a second series of continuous lines shat do not intersect each others, and said third repertoire of single-chain polypeptides present on the surface in a third series of continuous lines that do not intersect each other, wherein each line of said first series

intersects with each line of said second and third series, each line of said second series intersects with each line of said first and third series, and each line of said third series intersects with said first and second series, such that members of the first, second, and third repertoires are juxtaposed to each other, thereby generating three-chain polypeptides at the intersection of said first, second, and third series of lines, thereby creating a combinatorial library of three-chain polypeptides.

With regard to the written description requirement, the attention of the Applicant is directed *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985)(quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)).

Additionally, it is noted that written description is legally distinct from enablement: "Although the two concepts are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of*

California v. Eli Lilly & Co. And also *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

In this case, the instant invention claimed method for making a broad genus of compositions, i.e. a combinatorial library of three-chain polypeptides, which represents enormous scope because the claims do not place any limitations on the number of atoms, i.e. binding moieties, types of atoms or the way in which said atoms can be connected together to form such a compound and/or composition (three-chain polypeptides). Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope encompassing virtually every known class and subclass of compounds (three-chain polypeptides). For example, Lehninger et al. disclose each protein has a specific chemical or structural function such that each protein has a unique three-dimensional structure (pg. 160, lines 4-6; fig. 7-1). The three-dimensional structure of a protein is determined by its amino acid, but the relationship between the amino acid sequence and the three-dimensional structure is an intricate puzzle that has yet to be solved in detail (see pg. 160, lines 14-29). Thus, virtually an infinite number of possibilities would be included in Applicants' claimed scope encompassing virtually every known class and subclass of compounds, i.e. three-chain polypeptides would encompass protein trimers such as collagen and α-Keratin.

Consequently, the scope of the instant claimed compositions, i.e. three-chain polypeptides, includes an enormous number of structural variants.

In contrast, the instant specification provided a broad generic definition of the term "polypeptides" (see pg. 28, lines 7-27) and is silent regarding the term "three-chain

polypeptides". The instant specification one example is directed to the method of three-dimensional screening using anti-BSA heavy chain, anti-BSA light chain, and BSA (see specification Example 7, pgs 55-56; fig. 9 and 11).

Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding adequate disclosure. For adequate disclosure, like enablement, requires ***representative examples***, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is ***substantial variation within the genus***, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

Here, the instant specification has only provided one working example of the claimed invention (i.e. the method of three-dimensional screening using anti-BSA heavy chain, anti-BSA light chain, and BSA). Thus, a person of skill in the art would not believe that Applicants were in possession of a genus that encompasses virtually an infinite number of compounds and/or compositions encompassing every class and subclass of the instant claimed method for making a combinatorial library of three-chain polypeptides, i.e. the product produce by the instant claimed method encompasses any protein trimers.

Accordingly, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the claimed invention. The instant specification and claims do not provide any guidance as to what changes should be made to extend the instant specification one example to the infinite number of possibilities that are currently being claimed composition, i.e. three-chain polypeptides, for use in the instant claimed method. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variable, the instant specification single example is insufficient to describe the enormous genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification does not teach the instant claimed method for making a combinatorial library of three-chain polypeptides, i.e. the product produce by the instant claimed method encompasses any protein trimers. Therefore, only the method of three-dimensional screening using anti-BSA heavy chain, anti-BSA light chain, and BSA, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

Conclusion

11. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
August 4, 2006

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